REMARKS

Claims 1-8 and 15 are currently pending in the Application. Claims 9-14 have been withdrawn.

Claim 1 has been amended to incorporate the limitations of claim 5. Support for this amendment can be found in claim 5 as originally filed and does not add any new matter to the Application.

Claim 5 has been cancelled.

Thus, after entry of this amendment, claims 1-4, 6-8, and 15 shall be pending in the Application.

Drawings

The Office Action asserts that although three sets of color drawings were submitted, a petition and appropriate fee were not submitted.

Applicants respectfully aver that both the petition and fee were submitted on March 24, 2004. As evidence of this, Applicants submit copies of the petition submitted March 24, 2004 and postcard listing the same stamped and returned by the U.S. Patent and Trademark Office (copies of petition and postcard attached hereto as Appendix A).

In view of these remarks, Applicants respectfully request entry of the previously submitted three sets of color drawings.

Claim Rejections – 35 U.S.C. § 102(b)

Claims 1-3 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Denderen et al., J. Exp. Med. 169:87-98, 1989 ("Denderen I") as evidenced by Fritz et al., PCT Publication No. WO/200269900 ("Fritz") Denderen et al., Leukemia and Lymphoma 11: 29-32, 1993 ("Denderen II"), and Arlinghaus et al., U.S. 5,369,008 ("Arlinghaus").

Applicants have overcome this ground for rejection with the present amendment to claim 1, clarifying that the claimed antibodies are monoclonal antibodies.

Denderen I alone, or as evidenced by Fritz, Denderen II, and/or Arlinghaus, nowhere teaches or even suggests a monoclonal antibody that specifically binds to human P210 BCR-ABL fusion protein (SEQ ID NO: 1), but does not bind wild type BCR or wild-type c-ABL.

Based on these amendments and remarks, Applicants respectfully request that this ground for rejection be reconsidered and withdrawn.

Claim Rejections – 35 U.S.C. § 103

Claims 1-7 and 15 stand rejected under 35 U.S.C. § 103 as being unpatentable by Denderen et al., J. Exp. Med. 169:87-98, 1989 ("Denderen I") as evidenced by Fritz et al., PCT Publication No. WO/200269900 ("Fritz"), Denderen et al., Leukemia and Lymphoma 11: 29-32, 1993 ("Denderen II"), and Arlinghaus et al., U.S. 5,369,008 ("Arlinghaus"), in view of U.S. 6,617,119 ("Prusiner").

Applicants respectfully traverse this ground for rejection.

The present claims require a monoclonal antibody that a monoclonal antibody that specifically binds to human P210 BCR-ABL fusion protein (SEQ ID NO: 1), but does not bind wild type BCR or wild-type c-ABL. None of the cited references, alone or in combination, teaches the monoclonal antibodies of the present claims. Nor do they, alone or in combination, suggest the claimed antibodies.

Denderen I, as evidenced by Fritz, Denderen II, and/or Arlinghaus, describes a polyclonal antibody that allegedly binds to a human BCR-ABL fusion protein. However, nowhere does Denderen I, as evidenced by Fritz, Denderen II, and/or Arlinghaus, teach or suggest a monoclonal antibody with the attributes of that covered by the current claims. Or does Prusiner cure this deficiency. Prusiner merely describes a polyclonal antibodies and monoclonal antibodies, both of which are specific to a conformation of a protein. Prusiner nowhere teaches or suggests an antibody, monoclonal or even polyclonal, that specifically binds to human P210 BCR-ABL fusion protein (SEQ ID NO: 1), but does not bind wild type BCR or wild-type c-ABL.

Thus, Applicants respectfully aver that the collective teachings of the cited references, namely Denderen I, Fritz, Denderen II, Arlinghaus, and Prusiner, are of a polyclonal antibody that allegedly binds to a human BCR-ABL fusion protein. Applicants respectfully aver that a polyclonal antibody cannot render a monoclonal antibody having the same specificity obvious to the ordinarily skilled artisan. The amount of time and effort involved in generating a monoclonal antibody is much larger than that required to generate a polyclonal antibody. Nor is there any

guarantee that a monoclonal antibody could be generated or, if such a monoclonal antibody could be generated, that its selectivity for its specific site would be higher than that of the polyclonal antibody. Were that the case, since the generation of monoclonal antibodies is very well known in the art (e.g., the inventors of the technique to generate monoclonal antibodies were awarded the Nobel Prize in 1984 for their efforts), all commercially available antibodies would be monoclonal antibodies.

However, many commercially available antibodies are polyclonal antibodies. Two examples of such commercially available polyclonal antibodies attached hereto as Appendix B (the 14-3-3ε Antibody from Cell Signaling Technology, Inc. and Appendix C (the Aak1 antibody from PeoSci Inc.). Numerous other polyclonal antibodies are commercially available. That these polyclonal antibodies are still for sale 25 years after a Nobel Prize was awarded for the technique of making monoclonal antibodies clearly attests to the fact that it is not obvious to attempt to make a monoclonal antibody with the same specificity as a polyclonal antibody, and certainly not obvious that such an attempt would be successful.

Accordingly, Applicants respectfully aver that none of Denderen I, Fritz, Denderen II, Arlinghaus, and Prusiner, either alone or in combination, can render the present claims unpatentable under 35 U.S.C. §103. Based on these remarks, Applicants respectfully request reconsideration and withdrawal of this ground for rejection.

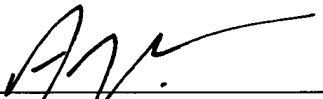
CONCLUSION

For all of the foregoing reasons discussed above, it is urged that the Application is in condition for allowance, an indication of which is respectfully solicited.

If there are any outstanding issues that might be resolved by an interview or an Examiner's amendment, the Examiner is requested to call Applicant's attorney at the telephone number shown below.

As mentioned above, accompanying this paper is a petition to revive an unintentionally abandoned application. To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper and/or in future communications, including extension of time fees, to Deposit Account No. 50-1774, Ref No: CST-214, and please credit any excess fees to such deposit account.

Respectfully submitted,



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awarner@cellsignal.com
(978) 867-2343

Dated: March 23, 2009

Appendix A

Express Mail Label No. E[illegible]69119339US
Date of Deposit: March 24, 2004

Attorney Docket No. CST-214
PAIR Customer No.: 31012

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Wetzel *et al.*

ASSIGNEE: CELL SIGNALING TECHNOLOGY, INC.

SERIAL NUMBER: Not Yet Assigned EXAMINER: Not Yet Assigned

FOR: ANTIBODIES SPECIFIC FOR BCR-ABL FUSIONS PROTEIN AND USES THEREOF

March 24, 2004
Beverly, Massachusetts

Mail Stop Patent Application
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO ACCEPT COLOR DRAWINGS OR PHOTOGRAPHS (37 C.F.R. 1.84 (a)(2) or (b)(2)).

1. This petition is for the acceptance of color drawings (37 C.F.R. § 1.84(a)(2)). A color drawing of Figure 4 is necessary in this application because black and white drawings do not have the contrast necessary to show the results depicted in the color drawings.

2. Attached hereto are three (3) sets of color photographs of FIG. 4 (3 sheets) and 1 black and white copy of the same figure (1 sheet).

3. The petition fee required under 37 C.F.R. § 1.17(h) is paid as follows:

   ☒ Attached is a check for the sum of $130.00.

   ☐ Please charge the petition fee of $130.00 to Deposit Account No. 50-1774, Ref. No. CST-214.

   ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 50-1774, Ref. No. CST–214.

4. The specification contains the required statement pursuant to 37 C.F.R. §1.84(a)(2)(iv).

A duplicate of this petition is attached.

Respectfully submitted,

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Intellectual Property Counsel
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166B Cummings Center
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Tel: (978) 867-2311

Serial No. Unknown File No. CST-214 By: JGC/smh

Title: Antibodies Specific for the BCR-ABL Fusion Protein and Uses Thereof

Application of Wetzel, et al Date: March 24, 2004

The U.S. PTO Mail Room acknowledges receipt of the following on the date stamped hereon:

[ ] Req. for CPA under 37 CFR 1.53(d)
[ ] Change of Attorney's Address
[X] New Power of Attorney w/Decl. (3 pgs.)
[X] Patent Application
[X] Non-provisional [ ] Provisional
Incl. 30 pages, (26 pgs) Specification,
(1 pgs) Abstract, (3 pgs) Claims (15 # claims)
[ ] Design Patent Application
[ ] Declaration(s) _____
[X] Drawings 4 sheet(s) (FIGS. 1 - 4)
[ ] Formal [X] Informal
[ ] Verified Statement claiming small entity status
[ ] Assignment and Cover Sheet

[ ] Provisional Application Cover Sheet
[ ] Inf. Discl. Statement, PTO Form 1449
[ ] References Cited
[ ] Copy of Notice to File Missing Parts
[ ] Amendment/Response
[ ] Petition for Ext. of Time (x2)
[ ] Issue Fee Transmittal
[ ] Letter to Official Draftsperson
[ ] Notice of Appeal
[ ] Brief (x3)
[X] Check for $370.00 Check # 037604
[X] Transmittal Letter (x2) (2 pgs.)
[ ] Cert. of Mailing under 37 CFR 1.8(a)
[X] Express Mail Label No. EU169119339US

[X] Other App. Cover Sheet (1 pg.); Req. for Filing a New Non-Provisional App. Under 37 C.F.R. §1.53(b) (3 pgs.); Sequence Listing (3 pgs.); Computer Readable copy of Sequence Listing (1 disk); Petition to Accept Color Drawings (6 pgs. including dupl. of Petition); Check for $130.00 (Check No. 037603)

DATE MAILED March 24, 2004

Serial No. Unknown File No. CST-214 By: JGC/smh

Title: Antibodies Specific for the BCR-ABL Fusion Protein and Uses Thereof

Application of Wetzel, et al Date: March 24, 2004

The U.S. PTO Mail Room acknowledges receipt of the following on the date stamped hereon:

[ ] Req. for CPA under 37 CFR 1.53(d)
[ ] Change of Attorney's Address
[X] New Power of Attorney w/Decl. (3 pgs.)
[X] Patent Application
[X] Non-provisional [ ] Provisional
Incl. 30 pages, (26 pgs) Specification,
(1 pgs) Abstract, (3 pgs) Claims (15 # claims)
[ ] Design Patent Application
[ ] Declaration(s) _____
[X] Drawings 4 sheet(s) (FIGS. 1 - 4)
[ ] Formal [X] Informal
[ ] Verified Statement claiming small entity status
[ ] Assignment and Cover Sheet

[ ] Provisional Application Cover Sheet
[ ] Inf. Discl. Statement, PTO Form 1449
[ ] References Cited
[ ] Copy of Notice to File Missing Parts
[ ] Amendment/Response
[ ] Petition for Ext. of Time (x2)
[ ] Issue Fee Transmittal
[ ] Letter to Official Draftsperson
[ ] Notice of Appeal
[ ] Brief (x3)
[X] Check for $370.00 Check # 037604
[X] Transmittal Letter (x2) (2 pgs.)
[ ] Cert. of Mailing under 37 CFR 1.8(a)
[X] Express Mail Label No. EU169119339US

[X] Other App. Cover Sheet (1 pg.); Req. for Filing a New Non-Provisional App. Under 37 C.F.R. §1.53(b) (3 pgs.); Sequence Listing (3 pgs.); Computer Readable copy of Sequence Listing (1 disk); Petition to Accept Color Drawings (6 pgs. including dupl. of Petition); Check for $130.00 (Check No. 037603)

DATE MAILED March 24, 2004

Appendix B

Cell Signaling TECHNOLOGY

Product Pathways - Tyrosine Kinase/ Adaptors

14-3-3 ε Antibody #9635

No.	Size	Price
9635S	100 ul (10 Western mini-blots)	please select country
custom	custom/drug discovery	email request

compare antibodies
control extracts

Applications	Reactivity	Sensitivity	MW (kDa)	Source
W	H M R Mk	Endogenous	28	Rabbit

Applications Key: W=Western Blotting
Reactivity Key: H=Human M=Mouse R=Rat Mk=Monkey
Species cross-reactivity is determined by Western blot.

Protocols

9635: Western Blotting

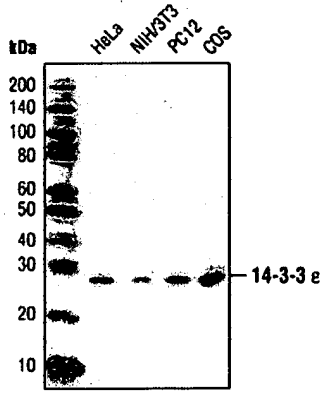
Specificity / Sensitivity

14-3-3 ε Antibody detects endogenous levels of total 14-3-3 ε protein.

Source / Purification

Polyclonal antibodies are produced by immunizing animals with a synthetic peptide (KLH-coupled) derived from the sequence of human 14-3-3 ε. Antibodies are purified by protein A and peptide affinity chromatography.

Western Blotting



Western blot analysis of extracts from various cell types using 14-3-3 ε Antibody.

Background

The 14-3-3 family of proteins plays a key regulatory role in signal transduction, checkpoint control, apoptotic and nutrient-sensing pathways (1,2). 14-3-3 proteins are highly conserved and ubiquitously expressed. There are at least seven isoforms, β, γ, ε, σ, ζ, τ and η that have been identified in mammals. The initially described α and δ isoforms are confirmed to be phosphorylated forms of β and ζ, respectively (3). Through their amino-terminal α helical region, 14-3-3 proteins form homo- or heterodimers that interact with a wide

variety of proteins: transcription factors, metabolic enzymes, cytoskeletal proteins, kinases, phosphatases and other signaling molecules (3,4). The interaction of 14-3-3 proteins with their targets is primarily through a phospho-Ser/Thr motif. However, binding to divergent phospho-Ser/Thr motifs, as well as phosphorylation independent interactions has been observed (4). 14-3-3 binding masks specific sequences of the target protein, and therefore, modulates target protein localization, phosphorylation state, stability and molecular interactions (1-4). 14-3-3 proteins may also induce target protein conformational changes which modify target protein function (4,5). Distinct temporal and spatial expression patterns of 14-3-3 isoforms have been observed in development and in acute response to extracellular signals and drugs, suggesting that 14-3-3 isoforms may perform different functions despite their sequence similarities (4). Several studies suggest that 14-3-3 isoforms are differentially regulated in cancer and neurological syndromes (2,3).

1. Muslin, A.J. and Xing, H. (2000) *Cell Signal* 12, 703-9.
2. Mackintosh, C. (2004) *Biochem. J.* 381, 329-42.
3. Dougherty, M.K. and Morrison, D.K. (2004) *J. Cell Sci.* 117, 1875-84.
4. Yaffe, M.B. (2002) *FEBS Lett.* 513, 53-7.
5. Bridges, D. and Moorhead, G.B. (2004) *Sci. STKE* 2004, re10.

Application References

Have **you** published research involving the use of our products? If so we'd love to hear about it. Please let us know!

Companion Products

- 9636 14-3-3 β/α Antibody
- 9637 14-3-3 γ Antibody
- 9638 14-3-3 τ Antibody
- 9639 14-3-3 ζ/δ Antibody
- 9640 14-3-3 η Antibody
- 7071 Phototope®-HRP Western Blot Detection System, Anti-rabbit IgG, HRP-linked Antibody
- 7074 Anti-rabbit IgG, HRP-linked Antibody
- 7720 Prestained Protein Marker, Broad Range (Premixed Format)
- 7727 Biotinylated Protein Ladder Detection Pack
- 7003 20X LumiGLO® Reagent and 20X Peroxide

This product is for *in vitro* research use only and is not intended for use in humans or animals. This product is not intended for use as therapeutic or in diagnostic procedures.

Appendix C

Catalog Number:
4831

Download Data Sheet
Download Printable Order Form

Antibody Production
Secondary Antibodies
Lysates

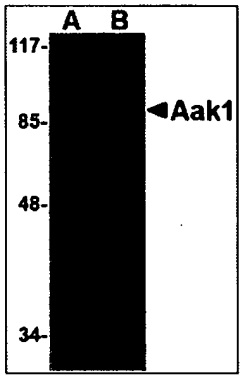
Pricing
0.1 mg $250.00
Add To Cart

Ordering Options
Website: PO # or Credit Card
Phone: 1-888-513-9525
Fax: 1-858-513-2692
Email: orders@prosci-inc.com

Primary Antibodies
Aak1 Antibody

Background
AP2-associated protein kinase 1 (Aak1) is a member of the Ark1/Prk1 subfamily of Ser/Thr protein kinases that are thought to regulate endocytosis by phosphorylating the accessory endocytic components. Aak1 interacts with and phosphorylates the mu2 subunit of the AP-2 complex, which promotes binding of the AP-2 to tyrosine based (Yxxf) internalization motif-containing receptors and subsequent receptor endocytosis. At least two isoforms of Aak1 are known to exist; the longer isoform contains an extended carboxy-terminus that contains an additional clathrin-binding domain. Overexpression of this long isoform or Aak1 depletion by RNA interference impairs transferrin recycling from the early/sorting endosome, suggesting that Aak1 functions at multiple steps of the endosomal pathway by regulating transferrin internalization and its recycling back to the plasma membrane.

Additional Names
Aak1 (CT), AP2-associated protein kinase 1



Description
Left: Western blot analysis of Aak1 in A-20 lysate with Aak1 antibody at (A) 1 and (B) 2 µg/ml.

Source
Aak1 antibody was raised against an 18 amino acid peptide near the carboxy terminus of the human Aak1.

Purification
Affinity chromatography purified via peptide column

Clonality / Clone
This is a polyclonal antibody.

Host
Aak1 antibody was raised in rabbit.

Please use anti-rabbit secondary antibodies.

Application
Aak1 antibody can be used for detection of Aak1 by Western blot at 1 – 2 µg/ml.

Tested Application
E, WB

Buffer
Antibody is supplied in PBS containing 0.02% sodium azide.

Storage
Aak1 antibody can be stored at 4°C, stable for one year. As with all antibodies care should be taken to avoid repeated freeze thaw cycles. Antibodies should not be exposed to prolonged high temperatures.

Positive Control

1. Cat. No. 1288 - A20 Cell Lysate

Species Reactivity
H M R

Protein Accession Number
NP_055726

This product belongs to the following categories:
- Antibodies
- Polyclonal Antibodies
- Signal Transduction Antibodies

Related Products
- A-20 Lysate
  (Catalog No. 1288).
- Aak1 Antibody
  (Catalog No. 4841).
- Aak1 Peptide
  (Catalog No. 4831P).

References

1. Connor SD and Schmid SL. Identification of an adaptor-associated kinase, AAK1, as a regulator of clathrin-mediated endocytosis. *J. Cell Biol.* 2002; 156:921-9.
2. Smythe E and Ayscough KR. The Ark1/Prk1 family of protein kinases. Regulators of endocytosis and the actin skeleton. *EMBO Rep.* 2003; 4:246-51.
3. Ricotta D, Connor SD, Schmid SL, et al. Phosphorylation of the AP2 m2 subunit by AAK1 mediates high affinity binding to membrane protein sorting signals. *J. Cell Biol.* 2002; 156:791-5.
4. Connor SD and Henderson DM. A novel AAK1 splice variant functions at multiple steps of the endocytic pathway. *Mol. Biol. Cell* 2007; 18:2698-706.

Datasheet 08-01W